

**REMARKS/ARGUMENTS*****Status of Claims***

Claims 1, 14, and 15 have been amended.

Claims 11-13, 16, and 20-29 have been canceled.

Claims 2-10, and 30-32 have been withdrawn.

Thus, claims 1-10, 14-15, 17-19, and 30-32 are currently pending in this application.

Applicants hereby request further examination and reconsideration of the presently claimed application.

***Claim Rejections – 35 U.S.C. § 112***

Claims 14 and 15 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Applicants have amended claims 14 and 15 to replace the phrase “such as” with the phrase “selected from the group consisting of.” Applicants respectfully request withdrawal of the rejections.

***Claim Rejections – 35 U.S.C. § 103***

Claims 1, 11-15, and 17-19 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Schwartz, et al., U.S. Patent No. 6,500,987 (hereinafter “Schwartz”) in view of Am Ende, et al., U.S. Patent No. 6,517,866 (hereinafter “Am Ende”). Claims 11-13 have been canceled. Claims 14 and 15 depend from claim 1 while claims 18 and 19 depend from claim 17. Thus, the pending claims stand or fall on the application of the cited references to independent claims 1 and 17. Applicants submit the pending claims are patentable over the prior art as (1) the Office Action fails to establish a *prima facie* case of obviousness and (2) one of ordinary skill in the art would not have a reasonable expectation of success in combining the cited references.

**1. The Office Action has not established a prima facie case of obviousness**

Applicants have amended claim 1 to incorporate the limitations of now canceled claims 11-13 and recite:

A process for the preparation of sertraline hydrochloride Form V comprising:

- a. suspending/dissolving sertraline acetate in suitable solvents;
- b. adjusting the pH of the mixture to a value of from 1 to 2 with aqueous hydrogen chloride at a temperature of 25°C;
- c. stirring the reaction mixture at 25°C; and
- d. isolating and drying under vacuum to obtain sertraline hydrochloride Form V.

*See supra.* Applicants' amended claim 1 recites the preparation of sertraline hydrochloride Form V from sertraline acetate. In claim 17 Applicants recite the limitation "suspending/dissolving sertraline base in acetic acid." *See supra.* In both claims 1 and 17 of the instant application an acetate moiety is present in the reaction mixture during formation of sertraline hydrochloride Form V. Applicants note that *Schwarz* exemplifies the preparation of sertraline hydrochloride Form V from sertraline free base. The Office Action asserts that the instantly claimed subject matter is obvious when the sertraline acetate of *Ann Ende* is substituted for the sertraline mandelate of *Schwarz* in preparation of the free base. The Office Action further asserts that one of skill in the art would be motivated to make this substitution "because sertraline acetate is an equivalent of sertraline mandelate." *See* Office Action, page 7. Applicants note that in Example 1 of *Schwarz*, subsequent to neutralization of sertraline mandelate with sodium hydroxide, the phases of the reaction mixture are separated and the free base as an oil is isolated. *See Schwarz*, column 9, lines 56-61. Applicants respectfully submit that in the first instance, Applicants' claimed subject matter

does not include a process step wherein sertraline free base is isolated after neutralization of sertraline acetate nor is such a step recited in the instant application. In order to arrive at the instantly claimed subject matter, one of ordinary skill in the art when carrying out the Office Action's proposed methodology would not merely substitute the sertraline acetate of *Ann Ende* for the sertraline mandelate of *Schwarz*. Instead, the ordinarily skilled artisan would at least have to additionally forgo isolation and separation of the free base from the acetate moiety as disclosed by *Schwarz*. The Office Action is silent as to a rationale that purports why one of ordinary skill in the art having substituted sertraline acetate for sertraline mandelate would further modify the disclosure of *Schwarz* to eliminate a process step (i.e., isolation of the free base). Absent a rationale for these multiple modifications of *Schwarz*, the Office Action has not established a *prima facie* case of obviousness. According to MPEP § 2143 "the key to supporting any rejection under 35 U.S.C 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Federal Circuit has stated that "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

## 2. *Modification of the cited references would not have a reasonable expectation of success*

Further, were the Office Action assertions correct regarding simple substitution of sertraline acetate for sertraline mandelate (*arguendo*), the sertraline acetate provided by *Ann Ende* when subjected to the methodology of *Schwarz* would result in removal of the acetate moiety by isolation of the free base in the organic phase as previously discussed. *Schwarz* discloses subsequent reaction

of the isolated free base to form various polymorphic forms of sertraline hydrochloride. In contrast, Applicants disclose the formation of sertraline hydrochloride Form V using sertraline acetate as a starting material as recited in claim 1 or by suspending/dissolving sertraline base in acetic acid as recited in claim 17. In both instant claims 1 and 17, Applicants claim the **acetate moiety is present throughout the process** as isolation of the free base is not instantly disclosed or claimed. Applicants remind the Examiner that polymorphs are specific crystalline forms of a compound. The exact polymorphic form crystallized may be influenced by any number of factors during the crystallization process including but not limited to solvent effects; the presence of impurities; the level of supersaturation from which material is crystallized; the temperature at which crystallization is carried out; the geometry of covalent bonds; and changes in stirring conditions. The ability of minor condition changes to influence the polymorphic form of the material isolated is further supported by the *Schwarz* reference which details a large number of examples relating to various polymorphs of sertraline hydrochloride, and the examples involve the use of similar, but not identical, reaction conditions. Given that *Schwarz* discloses isolation of the free base from sertraline mandelate prior to formation of sertraline hydrochloride Form V, one of ordinary skill in the art would not have a reasonable expectation of success in isolating sertraline hydrochloride Form V from a reaction mixture having the acetate moiety as a component of the reaction mixture. According to MPEP § 2143.02 a reasonable expectation of success is required for a finding of obviousness. Citing to *in re Merck & Co., Inc.*, MPEP § 2143.02 notes “[t]he prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success (800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986)).”

In consideration of the foregoing, Applicants respectfully submit the pending claims are patentable over the cited references and request withdrawal of the rejections and allowance of the pending claims.

### CONCLUSION

Consideration of the foregoing amendments and remarks, reconsideration of the application, and withdrawal of the rejections are respectfully requested by Applicants. No new matter is introduced by way of the amendment. It is believed that each ground of rejection raised in the Office Action dated March 31, 2009 has been fully addressed. If any fee is due as a result of the filing of this paper, please appropriately charge such fee to Deposit Account Number 50-1515 of Conley Rose, P.C., Texas. If a petition for extension of time is necessary in order for this paper to be deemed timely filed, please consider this a petition therefore.

If a telephone conference would facilitate the resolution of any issue or expedite the prosecution of the application, the Examiner is invited to telephone the undersigned at the telephone number given below.

Respectfully submitted,  
CONLEY ROSE, P.C.

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